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EXAMINER	
MCKENZIE, THOMAS C	
ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 01/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/518,501	ERION ET AL.	
	Examiner	Art Unit	
	Thomas McKenzie, Ph.D.	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18,20-46,48-57,150-153,155-157,165,166 and 171-174* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18,20-46,48-57,150-153,155-157,165,166 and 171-174* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1 2/2 2/2 12/3* 12/3 2/4 TCM
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to amendments filed on 10/28/04. Applicant has amended claim 4. Claim 174 is new. There are sixty-eight claims pending and sixty-eight are under consideration. Claims 1-16, 17-46, 48-57, 165, and 171-174 are compound claims. Claims 150-153, 155-157 are method of preparation claims. All claims were previously rejected. The application concerns some cyclic phosphate amides and preparations thereof. This is the fifth action on the merits.

Continued Examination Under 37 CFR 1.114

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/28/04 has been entered.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Structure of Radical M

Claims 1-3, 7, 9, 11-18, 20-46, 48-53, 56, 150-153, 155-157, 165, 166, and 171-173 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for

failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase in lines 20-21, page 2, claim 1, "M is selected from ... is a biologically active agents but is not an FBPase inhibitor" is indefinite. What is the structure of radical M? What do Applicants intend by "biologically active agent? How active and active as what? The phrase also occurs in claims 150, 166, `171, 172, and 173.

The Examiner suggests using chemical formulas to define the structure of the claimed "M" radical.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 7, 9-18, 20-46, 48-53, 150-153, 155-157, 165, 166, and 171-173 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way to convey reasonably to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The issue concerning the meaning of phrase "M is selected from ... is a biologically active agents but is not an FBPase inhibitor" is discussed above. Claims 1-3, 7, 9-18, 20-46, 48-53, 150-153, 155-157, 165, 166, and 171-173 do not contain a complete generic formula.

According to the MPEP §2163 I. A. "the issue of a lack of adequate written description may arise even for an original claim when an aspect of the claimed invention has not been described with sufficient particularity such that one skilled in the art would recognize that the applicant had possession of the claimed invention. The claimed invention as a whole may not be adequately described if the claims require an essential or critical feature which is not adequately described in the specification and which is not conventional in the art or known to one of ordinary skill in the art." The MPEP states in §2163 II 3 ii) "The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice (see i)(A), above), reduction to drawings (see i)(B), above), or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus (see i)(C), above). See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406." Applicants have made no assertion that there is any correlation between the biological function of radical "M" and its structure.

As discussed above the phrase ""M is selected from ... is a biologically active agents but is not an FBPase inhibitor" is not art recognized in synthetic organic chemistry. According to the MPEP §2163.02 Standard for Determining Compliance With the Written Description Requirement,

> "The courts have described the essential question to be addressed in a description requirement issue in a variety of ways. An objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed". *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). Under *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention, and that the invention, in that context, is whatever is now claimed. The test for sufficiency of support in a parent application is whether the disclosure of the application relied upon "reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter". *Ralston Purina Co. v. Far-Mar-Co., Inc.*, 772 F.2d 1570, 1575, 227 USPQ 177, 179 (Fed. Cir. 1985) (quoting In *re Kaslow*, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983))."

Thus, the chemist of ordinary skill in the art, who would make Applicants' compounds, would not know what "M is selected from ... is a biologically active agents but is not an FBPase inhibitor". That chemist would not have understood the inventor to be in possession of the claimed compounds at the time of filing.

This case was filed before Applicants had a clear idea of the structures of their desired compounds, how to make their compounds, and use the compositions

made from them. The specification provides broad areas of future research and speculation, inviting undue experimentation in learning how to use Applicants' invention. Applicants may well now be developing practical applications of their compounds, but the question here is what application they possessed at the time of filing. Anything is possible but as the U.S. Patent and Trademark Office, Board of Patent Appeals and Interferences wrote in *Bindra v. Kelly*, 206 USPQ 570 "*Probable* utility does not establish practical utility. Practical utility can, in our view, be established only by actual testing therefore, or by establishing such facts as would be convincing that such utility could be "foretold with certainty." *Blicke v. Treves*, supra, 112 USPQ at 475."

Applicants are reminded of what the U.S. Court of Appeals Federal Circuit wrote in *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398, "In claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus." "A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See *Fiers*, 984 F.2d at 1169-71, 25 USPQ2d at

1605-06 (discussing Amgen). "It is only a definition of a useful result rather than a definition of what achieves that result." "The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.")".

5. Claims 1-3, 7, 9-18, 20-46, 48-53, 150-153, 155-157, 165, 166, and 171-173 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making the compounds of dependant claims 4-6, 8, 10, 54, 55, 57, and 174, does not reasonably provide enablement for making all compounds where M is defined in claim 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. "The factors to be considered [in making an enablement rejection] have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims", *In re*

Rainer, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150, *Ex parte Formal*, 230 USPQ 546. a) Preparing any particular compound would first require ascertaining the structure of the M radical, devising a synthesis of the substance, and performing the required synthesis in the laboratory. This is an open-ended and potentially inconclusive degree of experimentation. b) The direction concerning synthesis is found in the passage spanning line 6, page 89 to line 32, page 98. This passage describes general procedures to be used with M radicals possessing specific functional groups, not every potential M radical. c) There are twenty-one working examples of synthesis of a compound of formula (I). This is found in the passage spanning line 28, page 103 to line 22, page 107 as well as line 12, page 111 to line 11, page 114. d) The nature of the invention is chemical synthesis, which involves chemical reactions.

e) The state of the art is that instructions to a pharmacologist or physician to search for some particular drug hardly constitute directions to the average BS organic chemist of how to make these compounds attached to Applicants cyclic phosphonamide array. f) The artisan using Applicants invention to prepare the claimed compounds would be a process chemist or pilot plant operator with a BS degree in chemistry and several years of experience. g) Chemical reactions are well-known to be unpredictable, *In re Marzocchi*, 169 USPQ 367, *In re Fisher*,

166 USPQ 18. h) The breadth of the claims includes all of the unknown number compounds of formula I.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to practice Applicants' invention.

The four arguments concerning the three rejections concerning the structure of M will be considered together. Firstly, Applicants argue that the skilled chemist understands the function of "biologically active agents". Secondly, Applicants reply upon the declaration of 1/24/04 to establish definiteness, written description, and enablement for their claims. Thirdly, Applicants argue that the radical M is not an essential feature of the claimed molecules. Fourthly, Applicants argue that functional language is permitted in patent claims.

This is not persuasive. Concerning the first point, there is no confusion about the function of M. What Applicants fail to address is the question of the unknown chemical structure of M.

Concerning the second point, the declarations were addressed in points #3-#8 of the previous office action.

Concerning the third point, Applicants' compounds are to be used for therapy. The phosphorus containing ring of formula I is not the moiety responsible for the pharmacological activity. Applicants admit that the molecule M-H is the active core. It is not logical that M is not essential for the function of Applicants' compounds since the compounds are to be used for therapy.

Concerning the fourth point, Applicants' claims are drawn to radicals formed from any drug with a specific biological property. What are the structures of these molecules and where in the specification do Applicants teach how to make this potentially limitless structural variety of such molecules? Case law is clear that such broad claims lack sufficient supporting description. Starting with a hormone case, which claimed a partially characterized peptide that was claimed in terms of its chemical properties, *In re Fisher*, 166 USPQ 18, the U.S. Court of Customs and Patent Appeals, wrote

> It is apparent that such an inventor should be allowed to dominate the future patentable inventions of others where those inventions were based in some way on his teachings. Such improvements, while unobvious from his teachings, are still within his contribution, since the improvement was made possible by his work. It is equally apparent, however, that he must not be permitted to achieve this dominance by claims which are insufficiently supported and hence not in compliance with the first paragraph of 35 U.S.C. 112. That

> paragraph requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art. In cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws. In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved. In the present case we must conclude, on the record before us, that appellant has not enabled the preparation of ACTHs having potencies much greater than 2.3, and the claim recitations of potency of "at least 1" render the claims insufficiently supported under the first paragraph of 35 U.S.C. 112.

This concept was expanded by the U.S. Court of Appeals Federal Circuit in *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.* 18 USPQ2d 1016 in a case concerning EPO genes. Since genes were held to be chemicals, the principle regarding enablement applies as well to all small molecules. The court held that:

> A gene is a chemical compound, albeit a complex one, and it is well established in our law that conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials, and to describe how to obtain it. See *Oka,* 849 F.2d at 583, 7 USPQ2d at 1171. Conception does not occur unless one has a mental picture of the structure of the chemical, or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by its principal biological property, e.g., encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property. We hold that when an inventor is unable to envision the detailed constitution of a

> gene so as to distinguish it from other materials, as well as a method for obtaining it, conception has not been achieved until reduction to practice has occurred, i.e., until after the gene has been isolated.

These two cases were quoted with approval in *Genentech Inc v. The Wellcome Foundation Ltd.*, 31 USPQ2d 1161 by the U.S. Court of Appeals Federal Circuit, which added further in a concurring opinion "Such a claim, defining a substance only by its function, encompassing all substances that accomplish that result, is akin to a single means claim, which might fail to satisfy the definiteness requirement of 35 U.S.C Section 112. See *Fiers v. Sugano*, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993)."

In *Fiers v. Sugano*, 25 USPQ2d 1601, U.S. Court of Appeals Federal Circuit repeated its views concerning the propriety of defining a chemical by its function and emphasized that for all chemicals including DNA "Claiming all DNA's that achieve a result without defining what means will do so is not in compliance with the description requirement; it is an attempt to preempt the future before it has arrived." They further required the inventor to have a "mental picture of the structure of the chemical, or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by its principal biological property."

Both *Fiers v. Sugano*, 25 USPQ2d 1601 and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.* 18 USPQ2d 1016 were quoted with approval by the U.S. Court of Appeals Federal Circuit in *Burroughs Wellcome Co. v. Barr Laboratories Inc.*, 32 USPQ2d 1915 who added,

> "An idea is definite and permanent when the inventor has a specific, settled idea, a particular solution to the problem at hand, not just a general goal or research plan he hopes to pursue. ... The conception analysis necessarily turns on the inventor's ability to describe his invention with particularity. Until he can do so, he cannot prove possession of the complete mental picture of the invention. These rules ensure that patent rights attach only when an idea is so far developed that the inventor can point to a definite, particular invention."

Prodrug

6. Claims 1-18, 20-46, 48-57, 150-153, 155-157, 165, and 171-173 remain rejected and claim 174 is newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In line 25, page 13, claim 1, Applicants claim "prodrug". The word "prodrug" is indefinite. The issue on second paragraph is whether the structures of the claimed compounds are clearly defined. Applicants' "prodrugs" are molecules whose structure lie outside the subject matter of formula I, but upon metabolism in the body are converted to active compounds falling within the structural scope of formula I. The claim

describes the function intended but provides no specific structural guidance to what constitutes a "prodrug". The word also occurs in claims 150, 171, 172, and 173.

The Examiner suggests deleting the word prodrug.

7. Claims 1-3, 7, 9-18, 20-46, 48-53, 150-153, 155-157, 165, 166, and 171-173 remain rejected and claim 174 is newly rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The word "prodrug" in line 25, page 13, claim 1, lacks written description. Applicants' claims are drawn to any derivative of the compounds of formula I with a specific biological property. What are the structures of these prodrugs? Structural formulas, names, or both can accurately describe organic compounds, which are the subject matter of claims 1-3, 7, 9-18, 20-46, 48-53, 150-153, 155-157, 165, 166, and 171-173. The issue was discussed above in the paragraph concerning written description of radical "M".

8. Claims 1-3, 7, 9-18, 20-46, 48-53, 150-153, 155-157, 165, 166, and 171-173 remain rejected and claim 174 is newly rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making the salts of the compounds of formula I, does not reasonably provide enablement for making

prodrugs of those compounds. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. Directions to a team of pharmacologist, medicinal chemists, and pharmacokinetics experts of how to search for Applicants prodrugs hardly constitute direction to the process chemist of how to make these claimed compounds.

"The factors to be considered [in making an enablement rejection] have been summarized as a) the quantity of experimentation necessary, b) the amount of direction or guidance presented, c) the presence or absence of working examples, d) the nature of the invention, e) the state of the prior art, f) the relative skill of those in that art, g) the predictability or unpredictability of the art, and h) the breadth of the claims".

a) Finding a prodrug is an empirical exercise. Predicting if a certain ester of a claimed alcohol, for example, is in fact a prodrug, that produces the active compound metabolically, in man, at a therapeutic concentration and at a useful rate is filled with experimental uncertainty. Although attempts have been made to predict drug metabolism *de novo*, this is still an experimental science. For a compound to be a prodrug, it must meet three tests. It must itself be biologically inactive. It must be metabolised to a second substance in a human at a rate and to

an extent to produce that second substance at a physiologically meaningful concentration. Thirdly, that second substance must be biologically active. Determining whether a particular compound meets these three criteria in a clinical trial setting requires a large degree of experimentation.

b) There is extensive discussion of the concept of prodrug and how to search for and prepare compounds of formula I that are themselves prodrugs. The direction concerning making the prodrugs, which liberate the compounds of formula, I is found in lines 13-16, page 30. This passage just states Applicants intent to do so. c) There is no working example of a prodrug which produces a compound of formula I. The biological data in the passage spanning line 10, page 115 to line 26, page 126 do not demonstrate that even any of the compounds of formula I are themselves prodrugs. The only *in vivo* experiments, Examples O-S appear to be prophetic and not working examples. d) The nature of the invention is clinical use of compounds and the pharmacokinetic behaviour of substances in the human body. e) The state of the prodrug art is summarized by Wolff (Medicinal Chemistry). The table on the left side of page 976 outlines the research program to be undertaken to find a prodrug. The second paragraph in section 10 and the paragraph spanning pages 976-977 indicate the low expectation of success. In that paragraph the difficulties of extrapolating between species are further developed.

Since, the prodrug concept is a pharmacokinetic issue, the lack of any standard pharmacokinetic protocol discussed in the last sentence of this paragraph is particularly relevant. Banker (Modern Pharmaceutics) in the first sentence, third paragraph on page 596 states that "extensive development must be undertaken" to find a prodrug. f) Wolff (Medicinal Chemistry) in the last paragraph on page 975 describes the artisans making Applicants' prodrugs as a collaborative team of synthetic pharmaceutical chemists and metabolism experts. g) The lack of predictability in finding prodrugs was discussed above. h) The breadth of the claims includes all of the hundreds of thousands of compounds of formula of claim 136 as well as the presently unknown list potential prodrug derivatives embraced by claim 136.

Thus, undue experimentation will be required to determine if any particular derivative is, in fact, a prodrug.

The five arguments concerning the three rejections concerning prodrug will be considered together. Firstly, Applicants correctly assert that the word "prodrug" occurs in many issued US patents. Secondly, Applicants argue that functional language is permitted in patent claims. Thirdly, Applicants assert that the skilled chemist "knows what a prodrug is". Fourthly Applicants rely upon the declaration of 1/25/04 to establish definiteness, written description, and enablement. Fifthly

Applicants express uncertainly as to which one of the eight *Wands* factors the examiner is relying upon for the conclusion of undue experimentation.

This is not persuasive. Concerning the first point, The U.S. Court of Customs and Patent Appeals held, *In re WAITE AND ALLPORT* 77 USPQ 586, "[w]e apprehend that there is no rule of patent law more firmly settled, nor any which has been more frequently stated, than the rule that this court will not allow rejected claims simply because similar claims may have been allowed by tribunals of the Patent Office in some other application, or even in the particular application under consideration. *In re Lee et al.*, 31 C.C.P.A. (Patents) 768, 139 F.2d 717, 60 USPQ 202, *In re Haller*, 34 C.C.P.A. (Patents) 1003, 161 F.2d 280, 73 USPQ 403." The indefiniteness remains despite what was allowed in another case. The U.S. Court of Customs and Patent Appeals wrote *In re Giolito* 188 USPQ 645: "We reject appellants' argument that the instant claims are allowable because similar claims have been allowed in a patent. It is immaterial whether similar claims have been allowed to others. See *In re Margaroli,* 50 CCPA 1400, 318 F.2d 348, 138 USPQ 158 (1963); *In re Wright*, 45 CCPA 1005, 256 F.2d 583, 118 USPQ 287 (1958); *In re Launder*, 41 CCPA 887, 212 F.2d 603, 101 USPQ 391 (1954)".

Concerning the second point, while functional language can be used in patent claims, the word "prodrug" lacks the critical attribute of possessing a clear, and well-understood connection between structure and function. That nexus must be present before a functional term can be used.

Concerning the third point, while the skilled chemist known what a prodrug is suppose to do, he most certainly does not know the structure of the derivate that conveys this property to any particular drug. He does not know what it "is", but rather what it "does".

Concerning the fourth point, the declarations were addressed in points #3-#8 of the previous office action.

Concerning the fifth point, the Examiner has inserted a listing of all eight *Wands* factors in the enablement rejection concerning "prodrug". The alphabetical index used in the listing corresponds to each point in the discussion. All eight *Wands* factors were considered in reaching the conclusion of undo experimentation. As stated in MPEP §2164.01(a) " It is improper to conclude that a disclosure is not enabling based on an analysis of only one of the above factors while ignoring one or more of the others. The examiner's analysis must consider all the evidence related to each of these factors, and any conclusion of nonenablement must be based on the evidence as a whole. 858 F.2d at 737, 740, 8

USPQ2d at 1404, 1407. A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). The determination that "undue experimentation" would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the above noted factual considerations. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404."

Negative Proviso

9. Claims 1-3, 7, 9-18, 20-46, 48-53, 150-153, 155-157, 165, 166, and 171-173 remain rejected and claim 174 is newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase in lines 21-22, page 13 "M is not -NH(lower alkyl), -N(lower alkyl)$_2$" is indefinite. M-PO_3^{-2} etc must be biologically active. Are $^{-2}O_3P$-NH(lower alkyl) or $^{-2}O_3P$-N(lower alkyl)$_2$ biologically active? If not, the proviso excluded something that is not present.

Applicants state that they excluded the amine radicals out of caution concerning the prior art and that they must understand the structure of M if they can exclude elements from M. While one can only admire Applicants caution concerning prior art, why omit something that is not included with in the definition of M? Why cause the present indefiniteness, if Applicants are so certain they understand the structures of all M-H compounds? Applicants would appear to be agreeing with the Examiner. Removing the proviso can easily solve this issue. The conclusion that the exclusion of certain elements from the set M means that all elements of the set M are understood is the categorical fallacy called composition. According to the online reader-built encyclopedia EvoWiki, "[y]ou commit this fallacy if you confuse the properties of the whole with the properties of a part".

Process

10. Claim 150 remains rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 150 provides for transforming "a compound drug having a $-PO_3^{2-}$ ...", but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced. All

the word "transforming" does is delineate which molecules are staring materials and which are products. No reactions are named. No reagents are named. No conditions essential for any successful chemical reaction are specified. What chemical reactions are being claimed?

The Examiner suggests adding the reagents and condition they intend to use to the claims.

Claim 150 remains rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd. App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Applicants argue that the claim is to be read in light of the specification and the skilled process chemist would understand how to effect the claimed process. This is not persuasive. Applicants point to a Mitsunobu reaction on page 94 and Examples 1 and 4 as defining their synthetic process. They argue that these reagents and conditions are the steps required to perform. If this is all that is intended, then why not place these reaction conditions into the claims. The claims measure the invention. The U.S. Court of Customs and Patent Appeals wrote *In re*

Priest, 199 USPQ 11 "We have consistently held that no applicant should have limitations of the specification read into a claim where no express statement of the limitation is included in the claim." *In re Prater*, 56 CCPA 1381, 1396, 415 F.2d 1393, 1405, 162 USPQ 541, 551 (1969)." The steps of a chemical process are the reagents and reactions required to affect the claim transformation. All Applicants have done is label what is the starting material and what is the product. No chemical steps are to be found in the claim.

Phosphorus chemistry is a narrow speciality not covered in either undergraduate organic chemistry or graduate organic synthesis classes. While the typical 1000-page undergraduate organic chemistry textbook contains a chapter on phosphorus chemistry, that chapter is invariably omitted during the yearlong course. Other than the Wittig and Emmons reagents for making olefins from carbonyl groups and the Mitsunobu reagent for functionalising alcohols, phosphorus-containing reagents are unfamiliar to the average chemist. The Wittig, Emmons, and Mitsunobu reagents contain phosphorus but the product of their use is phosphorus-free. Synthesis of phosphorus-containing compounds like Applicants' Formula I are simply beyond the training and experience of the average skilled synthetic chemist.

Evidence of the amount of phosphorus chemistry knowledge possessed by the average chemist is provided by Reusch (Virtual Text of Organic Chemistry). This text discusses only three topics in phosphorus chemistry, Nucleophilicity of Phosphorus Compounds, Oxidation States of Phosphorus Compounds, and Phosphorus Compounds as Reducing Agents. None of these three topics has anything to do with transforming $M\text{-}PO_3^{-2}$ into Formula I. Evidence of the topics covered in the typical graduate level advanced organic chemistry course is provided by Evans (Chemistry 206 Advanced Organic Chemistry). While there is a single lecture on silicon chemistry, there is no lecture devoted to phorphorus chemistry. None of the other specialized lectures appear to involve any phorphorus chemistry at all.

Thus, other than the chemical steps found in the specification the skilled chemist would not know how to make Applicants' Formula I.

Conclusion

11. Information regarding the status of an application should be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system,

contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free). Please direct general inquiries to the receptionist whose telephone number is (703) 308-1235.

12. Please direct any inquiry concerning this communication or earlier communications from the Examiner to Thomas C McKenzie, Ph. D. whose telephone number is (571) 272-0670. The FAX number for amendments is (571) 273-8300. The PTO presently encourages all applicants to communicate by FAX. The Examiner is available from 9:00am to 5:30pm, Monday through Friday. If attempts to reach the Examiner by telephone are unsuccessful, please contact James O. Wilson, acting SPE of Art Unit 1624, at (571)-272-0661.

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